

## High-throughput Target ID

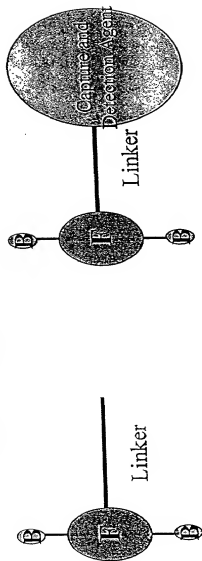
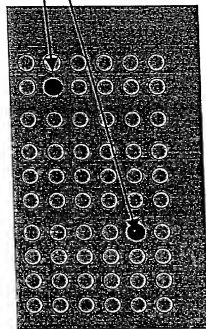
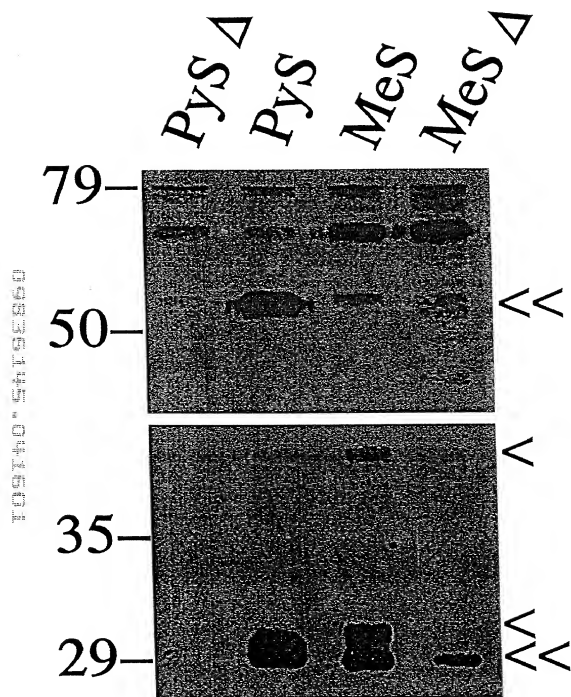
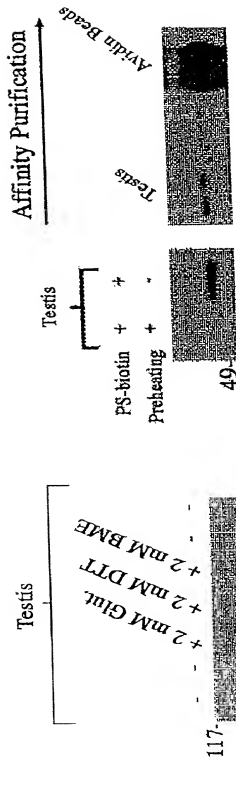
Library of Bioactive  
CompoundsLibrary of Target ID  
CompoundsUse corresponding  
activity-based probe to  
identify the biological target

FIGURE 2



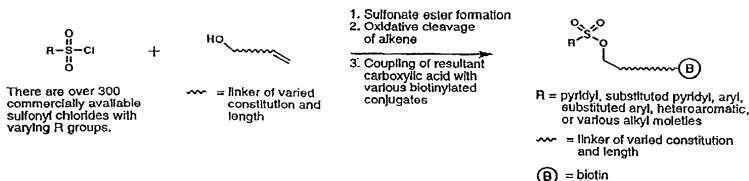
# Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes



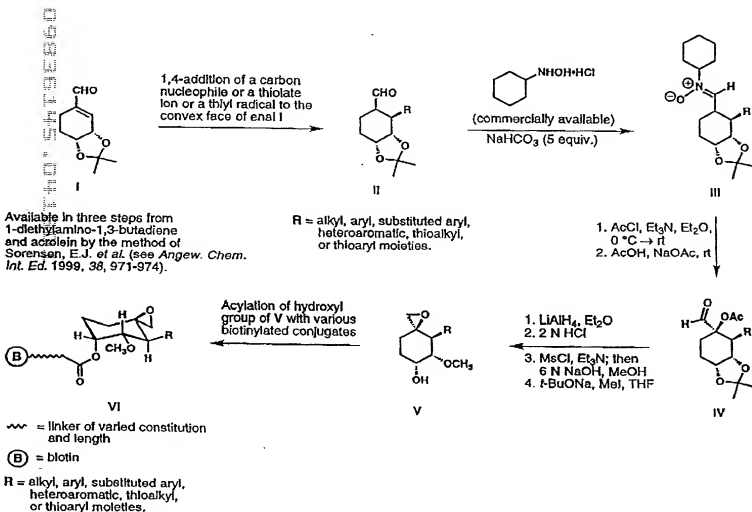
- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)
- 28 ADHs in fly genome
  - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 3

FIGURE 4



Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I → II → III → IV → V can be found in Sørensen, E.J. *et al. Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

# FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed
- FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes

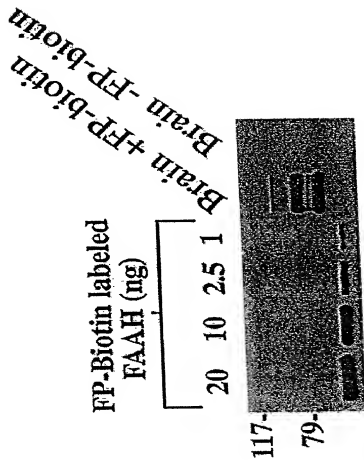
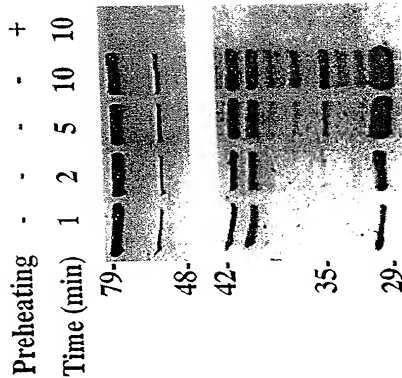


FIGURE 5

# Utility of Multiplexed probes in identifying Serine Hydrolases

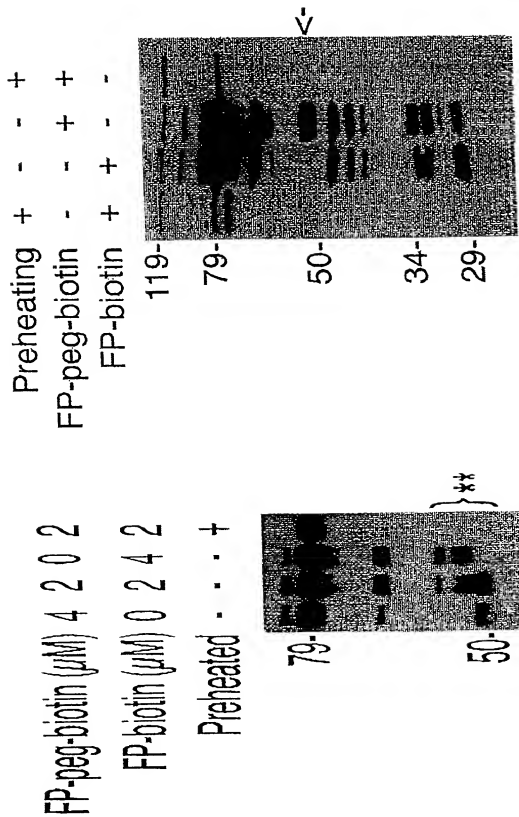


FIGURE 6.

FIGURE 7

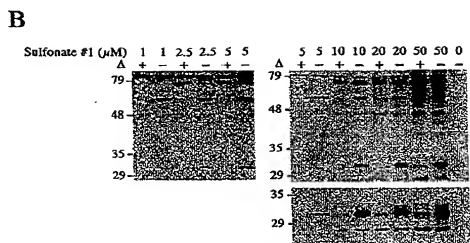
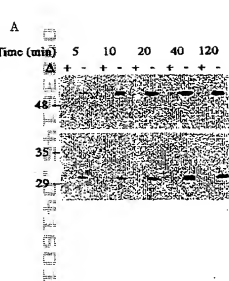
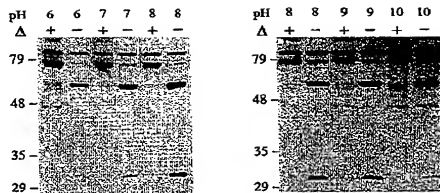


FIGURE 7

C



D

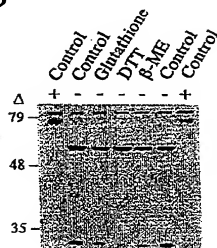




FIGURE 8

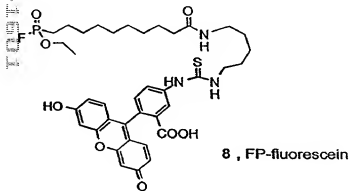
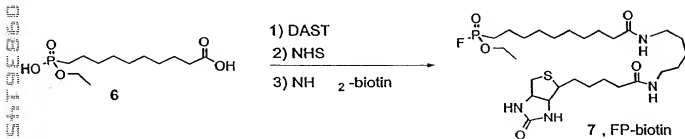
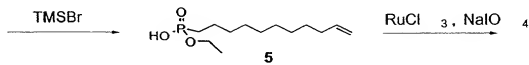
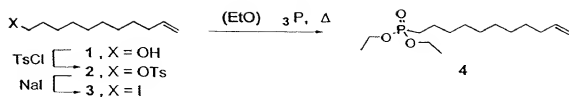


FIGURE 9

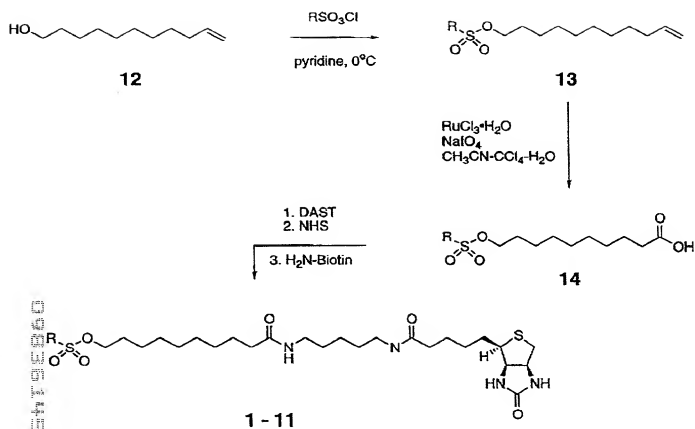
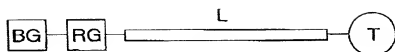
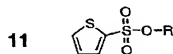
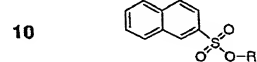
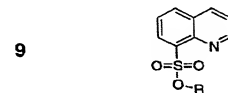
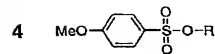
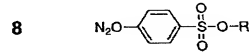
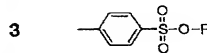
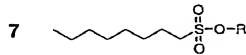
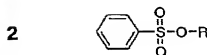
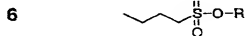
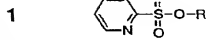
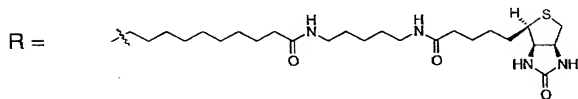


FIGURE 10

A.



B.



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**Su**

# B

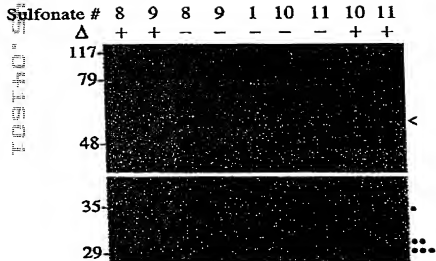
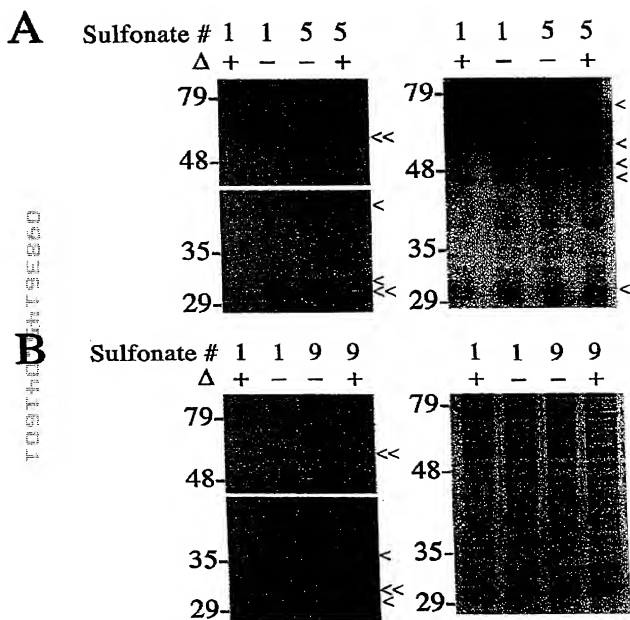
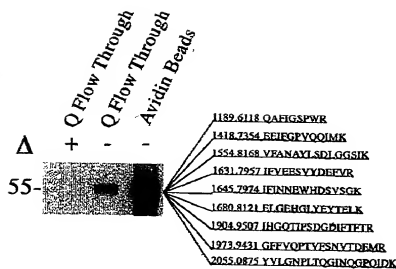


FIGURE 12

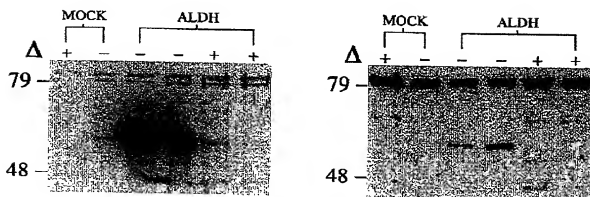


A

FIGURE 13



B



C

BL-21 Cells - - + +  
Testis Proteome + + - -  
 $\Delta$  + - + -

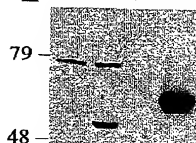
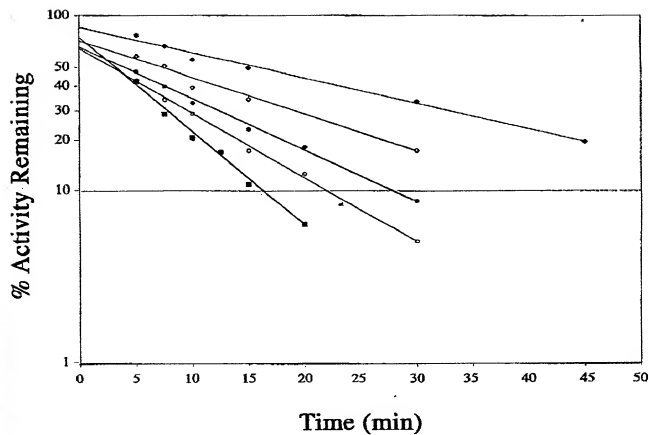


FIGURE 14

A

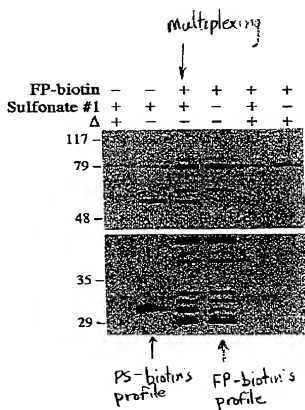


B

Competitor #	-	-	15	17	16	15	17	16
[Competitor ( $\mu$ M)]	0	0	5	5	5	50	50	50
$\Delta$	+	-	-	-	-	-	-	-



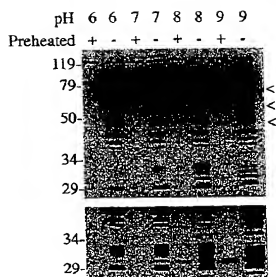
FIGURE 15



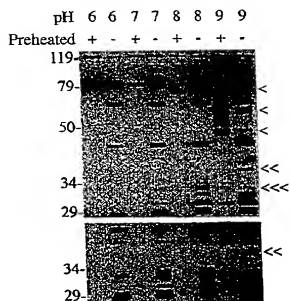
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FIGURE 16



FP-peg-biotin



FP-biotin

FIGURE 17

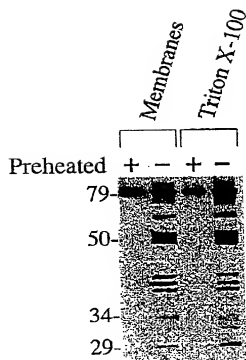


FIGURE 18

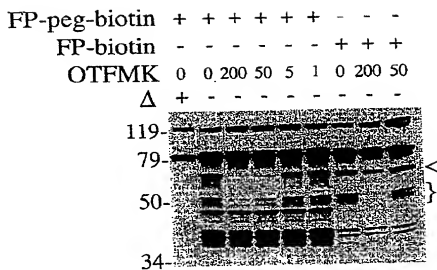


FIGURE 19

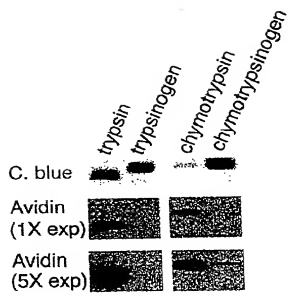


FIGURE 20

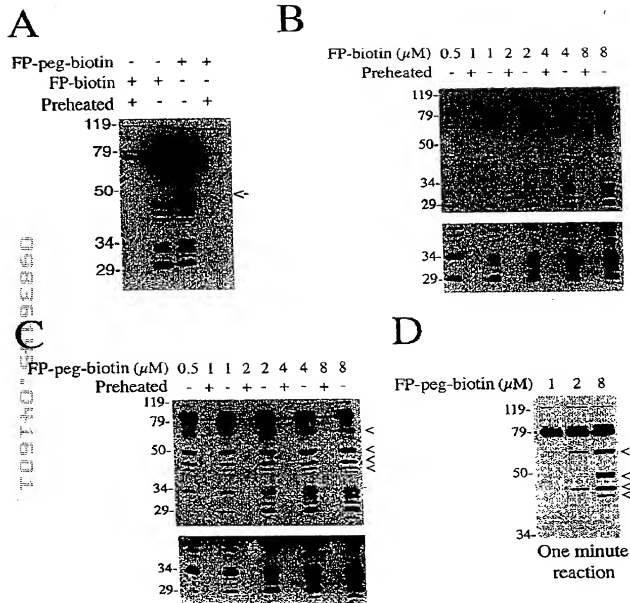


FIGURE 21

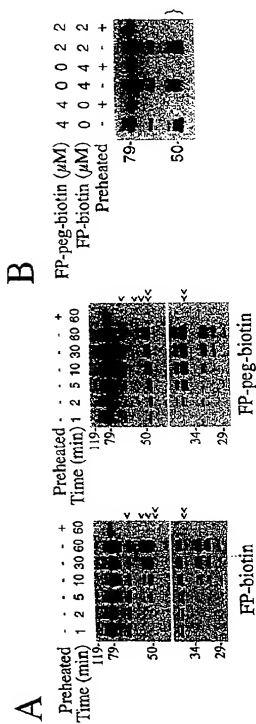
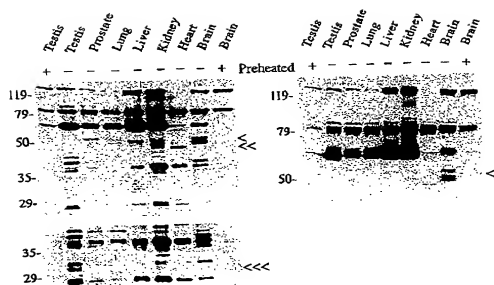


FIGURE 22



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FIGURE 23

